46. (amended) The method of claim 44, wherein the compound has at least 30% amino acid sequence homology to the amino acid sequence Gly-His-Lys-His-Lys-His-Gly-His-Gly-His-Gly-Lys-His-Lys-Asn-Lys-Gly-Lys-Lys-Asn-Gly-Lys-His-Asn-Gly-Trp-Lys-Thr (SEQ ID NO:6).

Remarks

Claims 1-4, 8, 9, 16, 19, 22 and 30-49 are pending in the application. Claims 1-4, 8, 9, 19, 22 and 30-35 stand rejected. Claims 16 and 3-49 are objected to. Reconsideration and allowance of the claims of the application is respectfully requested in view of the above changes and the following remarks.

Claim 30 has been rejected as indefinite for lack of a definition of X. A definition has been inserted. The definition finds support in the specification, page 4, lines 1-28. The amendment overcomes the indefiniteness rejection of claim 30, and its dependent claim 33.

Claim 30 has been objected to because the recited formula in the claim does not have a SEQ ID NO: for the entire sequence X_1-His-Lys-X-Lys-X_2. A sequence identifier is not required for the entire sequence stated in claim 30 since the scope of the claim is not limited to a single sequence of fixed length. Within the generic peptide X_1-His-Lys-X-Lys-X_2, X_1 may be (i) the specific 12-amino acid sequence SEQ ID NO:1, or (ii) an N-terminal truncation fragment of SEQ ID NO:1 containing at least one amino acid. X_2 may be (i) zero amino acids, (ii) the specific 12-amino acid sequence SEQ ID NO:2, or (ii) a C-terminal truncation fragment of SEQ ID NO:2 containing at least one amino acid. Thus, X_1 may represent from 1 to 12 amino acids, and X_2 may represent from zero to 12 amino acids. It is not possible to ascribe a single sequence identifier to the X_1-His-Lys-X-Lys-X_2, because of the variability of the sequence length and composition. The sequence listing requirements do not apply to the generic peptide X_1-His-Lys-X-Lys-X_2.

Claims 19, 22, 30-35, 41 and 46 are rejected under 35 U.S.C. 112, second paragraph. According to the Examiner, claims 19 and 22 are indefinite because of the missing article "a". These claims have now been amended by inserting "a".

According to the Examiner, claims 34 and 35 are indefinite as possibly depending from unidentified claims. The instant amendment to these claims is presumed to obviate any possible confusion; the claimed compounds are not "the same as recited in the preceding claims".

According to the Examiner, claims 41 and 46 are indefinite for the recitation of "at least *about*". Although applicant believes that the Examiner is incorrect about her interpretation of this phrase as broadening the range of "at least," because this phraseology simply signifies a minimum range wherein the range begins with the approximation "about x%", applicant has amended these claims by deleting "about".

Claim 1-4, 8-9 and 30-32 are rejected under 35 U.S.C. 102(b) over Ferreira et al. Examiner incorrectly maintains that the scope of the peptide claimed in claims 1 and 30 includes the nonapeptide Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val (SEQ ID NO:113). The rejection is based upon an incorrect interpretation of applicant's claims.

Claim 1 defines a peptide of the formula X_1-His-Lys-X-Lys-X_2 wherein X_1 is the segment His-Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly (SEQ ID NO:1), or an N-terminal truncation fragment thereof *containing at least one amino acid.*" The expression "N-terminal truncation fragment" is defined at page 9, lines 29-28 as "a fragment obtained from a parent sequence by removing one or more amino acids *from the N-terminus thereof*". The truncation operation starts at the N-terminal end of SEQ ID NO:1 (indicated by the arrow in Table 1, below), and proceeds in the C-terminal direction removing one, two, three, etc. amino acids until one amino acid remains.[1] The truncation possibilities are thus represented by the set of sequences of Table 1:

---

[1] This truncation operation is a conceptual picture to assist in the understanding of the term "fragment". This does not mean, however, that these peptides are necessarily prepared N-terminal or C-terminal digestion of a larger parent peptide by cleaving 1, 2, 3, ... amino acids from the parent. Rather, fragments can also be prepared, for example, by conventional solution-phase peptide synthesis (see, e.g., specification, page 12, line 28 – page 13, line 3). Thus, the term "fragment", as defined in the specification at page 9, line 29 – page 10, line 2, should be viewed conceptually as a peptide which is related to a large sequence by the absence of one or more amino acids from at least one end of the parent, not as a peptide that must be physically synthesized by digestion of a larger peptide..

Table 1

→ His-Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly
Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly
His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly
Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly
Gln-Gln-His-Gly-Leu-Gly-His-Gly
Gln-His-Gly-Leu-Gly-His-Gly
His-Gly-Leu-Gly-His-Gly
Gly-Leu-Gly-His-Gly
Leu-Gly-His-Gly
Gly-His-Gly
Gly

The smallest N-terminal truncation fragment is one amino acid. Contrary to Examiner's assertion that the claims "do not specify what amino acid residue the one has to be", it is abundantly clear from Table 1 that the "*one*" **must be Gly, and nothing else**.

Once again, it is respectfully submitted that truncating SEQ ID NO:1 from the N-terminus to the maximum extent possible - i.e., leaving only one original amino acid of SEQ ID NO:1 – results in the single amino acid Glycine (Gly) as X_1. Thus, X_1 as defined in amended claim 1 must always contain at a minimum the amino acid Glycine. The claimed peptide is characterized by the *minimal* sequence **Gly**-His-Lys-X-Lys. X_1 can never be zero amino acids, since this ignores the minimum placed on the length of the N-truncation fragment - "*containing at least one amino acid*".

Claims 1 and 30 are not anticipated by the Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val (as SEQ ID NO:113) peptide of Ferreira et al for yet another reason. X_2 in applicant's X_1-His-Lys-X-Lys-X_2 peptide is (i) zero amino acids, (ii) the specific 12-amino acid sequence SEQ ID NO:2, or (ii) a C-terminal truncation fragment of Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His-Val (SEQ ID NO:2) containing at least one amino acid. The C-terminal truncation fragments are generated by a truncation operation which starts at the C-terminal end of SEQ ID NO:2 (indicated by the arrow below), and proceeds in the N-terminal direction removing one, two, three, etc. amino acids until one amino acid remains. The truncation possibilities are thus represented by the set of sequences of Table 2:

Table 2

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His-Val←

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln

Leu-Asp-Asp-Asp-Leu-Glu-His

Leu-Asp-Asp-Asp-Leu-Glu

Leu-Asp-Asp-Asp-Leu

Leu-Asp-Asp-Asp

Leu-Asp-Asp

Leu-Asp

Leu

To correspond to Ferreira's nonapeptide, applicant's X_2 must be two amino acids. But it is clear from Table 2 that when X_2 is two amino acids in the claimed peptides, that two-amino acid sequence must be **Leu-Asp**. The corresponding two-amino acid sequence in the Ferreira nonapeptide is ***Asn-Val***. Similarly, for applicant's X_1 to correspond to Ferreira's nonapeptide, applicant's X_1 must consist of three amino acids. From Table 1, the three-amino acid sequence in the claimed peptides must be ***Gly-His-Gly***. The corresponding three-amino acid sequence in the Ferreira nonapeptide is **Glu-Ala-Pro**. The resulting claimed and Ferreira peptides are thus compared as follows:

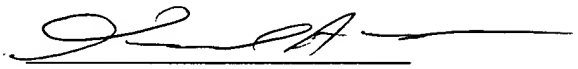
claimed	Gly-His-Gly-His-Lys- X -Lys-Leu-Asp
Ferreira.	Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val

It should be abundantly clear from the foregoing that Ferreira does not anticipate claims 1-4, 8-9 and 30-32. Reconsideration and withdrawal of the Section 102 rejection is earnestly solicited.

In conclusion, applicant believes that his claims contain patentable subject matter in appropriate form, and, therefore, the reconsideration and withdrawal of all objections and rejections and allowance of all claims are earnestly solicited.

Respectfully submitted,

KEITH R. McRAE



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APPENDIX A: Mark-up of Claims

19. (amended) A method of inhibiting angiogenesis comprising administering to a mammal an effective amount of a two-chain high molecular weight kininogen.

22. (amended) A method of inhibiting angiogenesis comprising administering to a mammal an effective amount of a single-chain high molecular weight kininogen.

30. (amended) A compound of the formula X_1-His-Lys-X-Lys-X_2 wherein

X is any amino acid,

X_1 is

the segment His-Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly (SEQ ID NO:1) , or N-terminal truncation fragment thereof containing at least one amino acid, and

X_2 is

(i) zero amino acids, or

(ii) the segment Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His-Val (SEQ ID NO:2), or C-terminal truncation fragment thereof containing at least one amino acid,

and wherein said compound optionally comprises an amino-terminal protecting group and optionally comprises a carboxy-terminal protecting group.

34. (amended) [The] A compound having the amino acid sequence Lys-His-Gly-His-Gly-His-Gly-Lys-His-Lys-Asn-Lys-Gly-Lys-Lys-Asn (SEQ ID NO:8).

35. (amended) [The] A compound having the amino acid sequence His-Lys-Asn-Lys-Gly-Lys-Lys-Asn-Gly-Lys-His-Asn-Gly-Trp-Lys-Thr (SEQ ID NO:9).

41. (amended) The method of claim 16, wherein the compound has at least [about] 30% amino acid sequence homology to the amino acid sequence His-Gly-His-Glu-Gln-Gln-His-Gly-

Leu-Gly-His-Gly-His-Lys-Phe-Lys-Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His-Val (SEQ ID NO:5).

46. (amended) The method of claim 44, wherein the compound has at least [about] 30% amino acid sequence homology to the amino acid sequence Gly-His-Lys-His-Lys-His-Gly-His-Gly-His-Gly-Lys-His-Lys-Asn-Lys-Gly-Lys-Lys-Asn-Gly-Lys-His-Asn-Gly-Trp-Lys-Thr (SEQ ID NO:6).